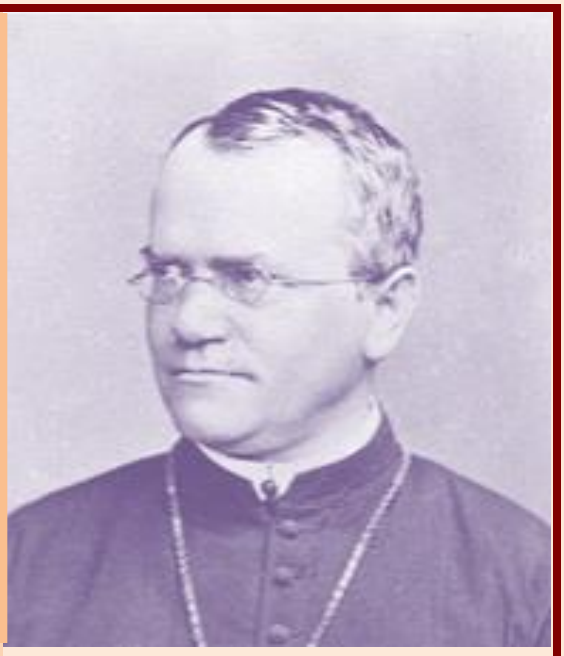
THE MENDEL NEWSLETTER

Archival Resources for the History of Genetics & Allied Sciences



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THE AMERICAN PHILOSOPHICAL SOCIETY
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The Mendel Newsletter

American Philosophical Society
Library & Museum
105 South Fifth Street
Philadelphia, PA 19106-3386
U.S.A.

www.amphilsoc.org/library

Editor
Michael Dietrich
Department of History and Philosophy of Science
1017 Cathedral of Learning
University of Pittsburgh
Pittsburgh, PA 15260
mdietrich@pitt.edu

Managing Editor
Adrianna Link
American Philosophical Society
alink@amphilsoc.org

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Photograph of Gregor Mendel, *ca.* 1860, from the Curt Stern Papers, American Philosophical Society. APS graphics:2210

From the Librarian

Patrick Spero

WHILE much of the world has had to close its doors due to the pandemic, I am happy to report that the Library & Museum, while certainly disrupted, has maintained an active acquisitions program. Since our last newsletter, the Society has acquired several papers that may be of interest to readers, including the papers of Francisco Ayala, Nina Jablonski, David Hungerford, and rare first editions of several of Darwin's works, some of which came as recently as this summer.

Longer-term, the Library & Museum just completed a two-year long review of its collection development policy. The Society has undertaken this review about every ten years. The revised policy highlights the Library's strength in genetics and identified the field as a key priority for collecting in the future. Its statement reads, in part, "Within the life sciences, the Library & Museum should continue focused collecting in those areas already strong – including genetics, evolution, and eugenics." The committee in charge of the history of science collecting area also highlighted evolutionary biology as an area of particular interest in the future.

In addition to its collection, the Library & Museum continues to build programming around the history of science. Such programming raises awareness of our collections, shares what is being discovered in them, and serves the Society's mission of promoting knowledge. In the past few years, we have added a long-term predoctoral fellowship to support research in the history of science, and we continue to host a large slate of short-term resident research fellows. We have also organized a number of events on the history of

science, including most recently a conference entitled "Evidence: The Use and Misuse of Data." Next year, we hope to open our exhibition, *Dr. Franklin, Citizen Scientist,* delayed due to the coronavirus pandemic. Our future programs include an exhibition on the history of climate science in 2022 and on women in science in 2023.

I hope you all will check out our website to see the range of virtual programs we currently offer and tune into some of them. In fact, if you have research from the APS's Library & Museum you'd like to share, you might consider presenting at our weekly brown bag lunches. And, by all means, please let us know about important papers that might be a good fit at the APS.

Celebrating Mendel's 200th Birthday July 22, 2022

M. Susan Lindee *and* John J. Mulvihill

mlindee@sas.upenn.edu John-Mulvihill@ouhsc.edu

MENDEL is a fascinating figure in the history of genetics, needless to say. His pea experiments are known to the average 6th grader. His status as a monk has been used to propose that religion and science are not in conflict. His quantitative results have been critiqued as too good to be true. And he is iconic, like Darwin: This is the *Mendel Newsletter* because Mendel's name is a legible shorthand for the entire history of modern genetics.

Johann Mendel was born July 22, 1822, and died as Abbot Gregor Mendel on January 6, 1884. As his 200th birthday looms, we have been thinking through options for how to recognize this important figure, and make sense of his historical and modern roles in genetics, meteorology, and agriculture.

While Lindee is presumably known to many readers of the *Mendel Newsletter*, Mulvihill probably is not. His commitments are those of a clinical geneticist in tune with history who wants the broader public and the scientific community to appreciate Mendel's contributions more accurately and completely.

A pediatrician and medical geneticist with 20 years' experience at the National Cancer Institute, he was chief of the Clinical Genetics Section of the Clinical Epidemiology Branch and Director of the Interinstitute Medical Genetics Program of the National Institutes of Health (NIH). In 1990, he became founder, chair, and professor of Human Genetics at the University of Pittsburgh. In 1998, he accepted the Children's Hospital Foundation--Kimberly V. Talley Chair of Genetics, Professor of Pediatrics, University of Oklahoma. In 2014, he became part-time consultant to the National Human Genome Research Institute.

Mulvihill's research has focused on the genetics of human cancer, with an emphasis on late genetic and reproductive effects in cancer survivors and on germ cell mutagenesis. Elected a Director of the American College of Medical Genetics, he is also a member of the Committee on Ethics, Law, and Society of the International Human Genome Organisation (HUGO) and a past Scientific Advisor of the Radiation Effects Research Foundation, Hiroshima and Nagasaki, Japan. While he is employed by Oklahoma, he is currently "on loan" to the National Human Genome Research Institute of the NIH, and he lives and works in Philadelphia.

The commemorative year is intended to pull together an international program of education and awareness for scientists and the public. Genetics as a scientific field has a history of huge public interest and stunning success, as well as historic abuses manifest in racist and eugenicist ideas. The program for 2022 will be, in Mulvihill's words, "conducted responsibly, with integrity, rigor, inclusion, innovation, and collaboration." Attention to the historical roles of Mendel can become a critical resource for thinking clearly about knowledge and religious communities, the origins of modern genetics and

agriculture, and the ethical questions raised by information about heredity today.

"Mendel's Research Garden," n.d from the Curt Stern Papers, American Philosophical Society, APSimg:507.

Working geneticists are an important audience for all events relating to this bicentennial of Mendel's birth. Mulvihill has even proposed that it might be useful, for publicity reasons, to discuss sequencing Mendel's DNA—with the resulting ethical debate itself of interest as a way of informing the public and the scientific community. He has established partnerships for this program with the two Mendel Museums in Brno, CZ, with scientific societies including the American Society of Human Genetics and the American Association for the Advancement of Science, with Jackson Laboratory and with several universities.

Roger Turner at the Science History Institute is working to develop meteorological perspectives on Mendel's life (Mendel collected significant meteorological data seen as relevant to agriculture); I am working with Section L of the AAAS to propose an event at the 2022 meeting that will explore Mendel and modern genetics.

As Mulvihill suggests, Mendel can be held as an exemplar of mentoring (in both directions, giving and taking). He was a nineteenth-century scientist who was able to thrive at the interdisciplinary interactions of botany, evolution, mathematics, physics, and agriculture. He contributed to improved fruit trees, ornamental flowers, horticulture, meteorology, and beekeeping. He also worked as a bank director, and was popular in his community of priests.

General knowledge of his work—inculcated first often in elementary school—might inspire public interest in this commemoration in ways that could productively call attention to enduring issues in the history of genetics. A broad discussion of Mendel's legacies could illuminate technical, social, ethical and moral concerns in the 200 years since his birth. Historians of science have a special contribution to make to this effort and are hereby invited to suggest options and ideas. Anyone interested should contact Susan Lindee, mlindee@sas.upenn.edu and John J. Mulvihill, John-Mulvihill@ouhsc.edu.

The Allan C. Wilson Papers at the Bancroft Library, University of California, Berkeley

Marina DiMarco
bancref@library.berkeley.edu

ALLAN C. Wilson was a University of California, Berkeley biochemist whose work in molecular evolution ranged from the timing of human-primate divergence and the production of Mitochondrial Eve to the isolation of ancient DNA from a Siberian wooly mammoth. The Wilson papers are available to researchers as part of the History of Science and Technology collection at the Bancroft Library of the University of California, Berkeley. These papers are an important source of material regarding the twentieth century development of molecular systematics, human genetics, the Human Genome Diversity project, and the history of the University of California.

Early life and training

Wilson was born in Ngaruawahia, New Zealand, on October 18, 1934 and grew up on the family dairy farm in Helvetia. Early on, he honed his talents for biological inquiry by careful observation of local birds (including a nearby ostrich farm) and by working to improve the family's cattle herd. Despite these bovine origins, his proud status as a New Zealander provoked a lifetime of sheep jokes and pranks from students and colleagues. (Wilson's use of a shepherd's crook to pull one of his particularly long-winded postdocs off a conference presentation stage did not help matters.)[1] Although some expected young Wilson to become a farmer or a veterinarian, he became interested in more general biochemical processes, and a local animal scientist convinced him to study zoology and chemistry at the University of Otago. Otago was far away and expensive, and Wilson took his BSc. there despite a great deal of financial hardship.

After graduation, Wilson traveled to the US to work with David S. Farner of Washington State University and to complete a MS in zoology working on hormonal regulation of bird behavior. From there, he went on to his doctoral work at the University of California, Berkeley, where he studied under Arthur Pardee. Pardee was a former student of Linus Pauling, perhaps best known for the famous 1959 PaJaMo (Pardee, Jacob, and Monod) paper on gene regulation in bacteria. After a postdoc with Nathan Kaplan at Brandeis, Wilson returned to Berkeley to set up his own lab in the biochemistry department, where he would spend the rest of his academic career.

[1] Cann (2014), p. 469.

Proteins, primates, and molecular clocks

Wilson was frustrated by what he perceived as the failure to synthesize molecular biochemical and population genetic approaches to the study of evolution. This frustration persisted throughout his career and motivated much of his work in the emerging field of Molecular Evolution. In his first year as a professor of biochemistry, Wilson met Vincent Sarich, an anthropology PhD student with whom he began work on an immunological clock for primate evolution. Sarich and Wilson's clock built on Emile Zuckerkandl and Linus Pauling's 1965 comparison of hemoglobin alpha chain sequences, which assumed a constant, universal rate of substitution in the amino acid sequence in order to estimate the time elapsed between evolutionary events from observed sequence differences.[2] Using serum albumin immunological reactivity to quantify differences between homologous proteins in human and primate populations, Wilson and Sarich (1967) put the divergence between humans and primates at about 5 million years prior. Wilson saw this as a methodological unification of molecular and population genetic approaches.

This use of molecular clocks had more in common with Zuckerkandl and Pauling's early work on molecular clocks than mere method. In "Molecules as Documents of Evolutionary History," (1965) Zuckerkandl and Pauling argued that molecules contained the greatest amount of a living organism's evolutionary history in an information theoretic sense, and that molecular semantides (DNA, RNA, and polypeptides) were the most certain or least "cryptic" sources of information about evolutionary history. They argued that the "most rational, universal, and informative molecular phylogeny will be built on semantophoretic molecules alone." Similarly, Wilson and Sarich (1969) argued that their molecular clock conferred greater certainty and objectivity than the comparatively fragmentary fossil record, and that a quantitative, molecular method should resolve controversy among anthropologists, paleontologists, and geneticists with regard to the timing of human-primate divergence.[3]

Such consensus was not forthcoming. Instead, this work provoked the first of many controversies throughout Wilson's career, as it contradicted other established paleoanthropological theories (for instance, the status of *Rampithecus* ape jaw fossils as a hominid).[4] Paleoanthropologists perceived Wilson and Sarich's work as an arrogant dismissal of their tradition, and they were not alone: creationists were also unhappy about the biochemical demonstration of similarity between humans and apes.[5]
Despite (or, more likely, because of) this controversy, Wilson continued to work on primate evolution, and together with student Mary-Claire King, he quantified the sequence similarity of human and chimpanzee proteins and DNA. In another landmark paper in 1975, King and Wilson proposed that gene regulatory differences, rather than sequence differences, explained the biological differences between the two.[6]

Mitochondrial Eve

Wilson wanted to extend the molecular clock to provide a temporal framework for

[2] For more on Zuckerkandl and Pauling and the development of molecular clocks, see Morgan (1998).

[3] For more on the status of "informational molecules" and the development of molecular evolution as a discipline, see Dietrich (1998), Suarez-Diaz (2007; 2009) and Sommer (2008; 2016).

[4] Klein and Takahata (2002), p. 238-239.

[5] Allan Wilson to Susan Smith, December 16, 1969. Allan Wilson Papers, Bancroft Library, University of California Berkeley (BANC MSS 95/22 c), microfilm edition (hereafter AWP), Series 3, Carton 5, Reel 13.

[6] King and Wilson (1975).

evolution, and this required new clock inputs. Because mitochondrial DNA (mtDNA) was a small molecule with a relatively rapid rate of mutation, mtDNA clocks made it possible to view evolutionary time in comparatively high resolution. Furthermore, mtDNA was thought to be exclusively inherited through the maternal line, and not subject to recombination; Wilson and colleagues thought this relatively simpler mode of inheritance made it a more reliable basis than nuclear DNA for evolutionary inference.[7] When Wes Brown joined the Wilson lab in the late 1970s, he brought with him from Caltech new techniques for isolating and amplifying mtDNA.[8] Building on Brown's (1980) work and new computational technologies like David Swofford's Phylogenetic Analysis Using Parsimony (PAUP) algorithm, Wilson's student Rebecca Cann built a restriction fragment length polymorphism (RFLP) mtDNA tree that identified an African single most recent common mitochondrial ancestor.[9] Mark Stoneking, another Wilson student, analyzed samples from Papua New Guinean populations to further calibrate the tree. In 1987, Cann, Stoneking, and Wilson published what became known as the "Out of Africa" tree, featuring an ancestor who quickly became known first as "African," and, later, as "Mitochondrial Eve."

Much like the human-primate divergence paper two decades before, this work sparked immediate scientific and popular controversy. At first, Wilson embraced the "African Eve" branding, hoping it would encourage others to take seriously the possibility that all modern humans originated in Africa. Later, however, it became a distraction from scientific criticisms, where advocates of the competing multiregional hypothesis used it to dismiss the result (which arguably contradicted their theory), and others argued that the population genetic assumptions needed to build and root the tree were suspect. In popular press, African Eve became a global celebrity, and much of the discussion centered around the notion of Eve as a first woman who was not just African, but Black. This reflected at least one common misconception about Mitochondrial Eve, who was by no means the first woman, but merely the last one to have her mitochondrial DNA survive in the population. It was also symptomatic of the reproduction of race in molecular evolution, where (despite Cann's protests) such trees were taken by some to show evidence of biological race differences, and where competing theories of human evolution routinely charged their adversaries with racism.[10]

Cann, Stoneking, and Wilson worked to address these criticisms and misconceptions, notably trying to rebrand Mitochondrial Eve as a "lucky mother," with little success. Although Mitochondrial Eve and the "Out of Africa" hypothesis are often touted as high points of Wilson's research career, neither Cann nor Wilson saw Mitochondrial Eve as entirely successful. Later work by Stoneking, Linda Vigilant, and other students in the Wilson lab lent additional support to the Out of Africa model using new sequence data and increasingly sophisticated computational methods, and after several years it was more widely accepted.[11] Meanwhile, Wilson worked to promote mtDNA techniques in his own lab and in his role as an associate

[7] For more on early nuclear DNA research in molecular evolution, see Marianne Sommer's account of the Cavalli-Sforza lab in *History Within* (2016).

[8] Brown and Vinograd (1974).

[9] Brown (1980), Cann et al. (1987).

[10] Notably, these included Wilson's former student and collaborator Vince Sarich, whose teachings and writings on race sparked outrage and protests on the Berkeley campus ("Campus LIfe"). Sarich's book, *Race: The Reality of Human Difference* is dedicated to Wilson (Sarich and Miele 2004).

[11] Vigilant et al (1991).

editor of the *Journal of Molecular Evolution.* priests.

Ancient DNA and PCR

In addition to his work to establish mtDNA as a basis for molecular clocks, Wilson was also at the forefront of development of techniques for isolating and amplifying so-called "ancient DNA," such as the mtDNA sequences from an extinct quagga and samples from a wooly mammoth.[12] Because Wilson had close connections to Cetus, he and his students not only helped to develop and calibrate polymerase chain reaction (PCR) protocols, but they were also among the first to bring PCR to bear on problems in molecular evolution. Together with Russell Higuchi and Svante Pääbo, Wilson worked to isolate DNA from museum collection specimens, including not only the quagga but also many birds, extinct zebras, and a 7,000 year-old human brain.[13] (Pääbo recalls an early prototype of a PCR machine made with washing machine valves routinely flooding the Wilson lab.)[14] Though Wilson is widely celebrated for the new molecular technologies he brought to bear on the study of evolution, in this sense, Wilson's approach was more continuous with the natural historical tradition in biology, and many of his students went on to appointments in natural history museums as well as biology research (although Wilson's opportunistic approach to sample acquisition, which included filling freezers with roadkill and instructing his young daughter Ruth in the art of getting New Zealand frogs through international customs on his behalf, might have appalled some natural historians).[15] This work on ancient DNA was an important starting point for molecular paleoanthropology, as well as for many forensic and medical applications. modern genetics.

Of immediate relevance was the importance of PCR for improving HIV testing and treatment in the late 1980s. At the height of the Reagan administration's escalation of the Cold War and its indifferent approach to the AIDS crisis, Wilson worked on PCR technologies that would facilitate HIV research, corresponded about collaborating with Cubans to identify human remains that were thought to belong to Christopher Columbus, and routinely protested nuclear weapons research policy at Berkeley.[16] Though Wilson is often described as a reserved character, he had no reservations about advocating for the inclusion of women as invited conference speakers (in a scathing letter to program organizers, he points out "Your program has no women"). He also had no trouble refusing to give a talk where he found the invitation of other speakers (South African scientists) politically distasteful.[17]

The Human Genome Diversity Project

Ancient DNA did not distract Wilson from his work on the relationships among contemporary human populations, where his interests expanded to include the evolution of cognition and the possible relationships between evolution, language, and the brain. In a 1989 presentation to the Merry Evolutionists informal discussion group, provoca-

[12] Higuchi et al (1984).

[13] Zagorski (2006).

[14] Andrews (2008).

[15] See Cann (2014), p. 467. For more on the continuity of the natural historical, experimental, and computational traditions in biology, see Strasser (2019). For more on the frogs, see Allan Wilson to Ruth Wilson, August 21, 1971, and Allan Wilson to Customs Officials, Auckland Airport, New Zealand, August 20, 1971. AWP Series 3, Carton 6, Reel 13, Frame 289.

[16] Schmeck (1985), Jonathan Ericson to Allan Wilson, April 21, 1987, AWP Series 3, Carton 8, Reel 21; Allan Wilson to Jonathan Ericson, October 19, 1987, AWP Series 3, Carton 8, Reel 21.

[17] Allan Wilson to Dr. Wilfried W. deJong, November 5, 1987. AWP Series 3, Carton 8, Reel 21.

tively titled, ``Eve and the Chomsky Mutation," Wilson drew on Luigi Cavalli-Sforza's work to hypothesize that the development of language could explain the migration out of Africa suggested by his mtDNA work with Cann, Stoneking, and others.[18] Though they had many intellectual disagreements, Wilson and Cavalli-Sforza joined forces to advocate for the Human Genome Diversity Project, an effort to collect and preserve DNA samples from isolated populations around the world. While Wilson, Cavalli-Sforza, and others saw this as a liberatory project which would celebrate human diversity, promote scientific inquiry, and move away from a Eurocentric conception of the human genome, many indigenous people and other advocates were skeptical of its anti-racist advertisement and critical of its implementation.[19]

Wilson did not live to participate directly in this final controversy. In late 1990, Wilson was diagnosed with leukemia, and he died July 21, 1991 while undergoing treatment in Seattle. His public call for the HGDP appeared posthumously in October 1991.[20] Wilson's former student, prolific research collaborator, and longtime lab manager, Dr. Ellen Prager, wrapped up operations in his lab. Wilson's many important methodological and theoretical contributions to molecular evolution and numerous prestigious fellowships and awards are only one part of his scientific legacy. His influence extends via his dozens of graduate students and postdocs, many of whom have made significant scientific contributions of their own, and also by way of the California biotechnology industry, of which he was a major advocate.[21]

The Wilson Papers

Dr. Ellen Prager organized Wilson's scientific papers for donation to the archive by Leona Wilson in 1994. Many papers and folders contain Prager's notes, which are often very informative. The Wilson papers contain 20 linear feet of material: 15 cartons, a box, one volume, and an oversized folder. Most of this material has been transferred to 50 reels of microfilm, which is the primary means of accessing the collection. Materials are arranged chronologically within each series, with notes from Dr. Prager estimating dates when they are absent. Papers Dr. Prager deemed confidential, such as letters of recommendation, have been removed.

The collection is arranged chronologically within several series, which are organized as follow. Series 1 contains publications 1957-1998. Series 2 contains materials related to manuscript preparation 1962-1992 (including rejected manuscripts with reviewer comments that may never have been published). Series 3 includes Wilson's professional correspondence 1959-1991; in addition to his students, Wilson's correspondents included Mayr, Howell, Lewontin, Dayhoff, Zuckerkandl, McCarthy, Fitch, Margoliash, Nei, Ohta, and many other major figures of twentieth century biology. Series 4 includes sabbaticals and special trips 1967-1989 and related correspondence (perhaps most notably, a reassuring note from home that his lab had not burned down in his absence during

[18] Allan Wilson, lecture notes, March 31, 1989. AWP Series 8, Carton 14, Reel 41, Frame 435. This lecture immediately followed Cavali-Sforza's address to the Merry Evolutionist society, a series which Wilson co-organized with Hy Harman.

[19] See M'Charek (2005 ab), Sommer (2016), and Reardon (2017). As Reardon (2017) notes, the HGDP became known as the Vampire Project because it was perceived as being more interested in the blood of indigenous people as research subjects than it was in the survival of indigenous communities. The controversy sparked by the HGDP has had lasting effects on both genome research and indigenous communities.

[20] Cavalli Sforza et al (1991).

[21] Allan Wilson to Senator John Garamendi, June 29, 1988. AWP Series 3, Carton 8, Reel 21.

Berkeley campus riots of 1969). Series 5 contains notes from lectures 1962-1990, both at Berkeley and elsewhere. Series 6 contains teaching materials 1965-1991. Series 7 contains documents from Wilson's education 1953-1962. Series 8, labeled "Professional 1956-1991," contains information on various career awards and honors, but also any publicity that Wilson kept about the lab, including several international news clippings. Series 9 contains material from Wilson's early career (1959-1971), and Series 10 contains research materials from 1965-1990. The final Series 11 contains notes, articles and letters concerned with Wilson's death and the fate of the lab, 1990-1994.

Accessing the Collection

More information on the Wilson Papers is available online: https://oac.cdlib.org/findaid/ark:/13030/kt958035w4/

The Wilson papers are located at the Bancroft Library of the University of California Berkeley in Berkeley, CA. Because some material may be stored offsite, it is important to contact the archives before visiting. Bring a USB drive to store microfilm scans on pain of being forced to buy one with a Berkeley logo on it.

The Johannes Holtfreter Papers at the Marine Biological Laboratory

Michael R. Dietrich
mdietrich@pitt.edu

THE archives of the Marine Biological Laboratory in Woods Hole, MA have made the papers of embryologist Johannes Holtfreter available to researchers. While the correspondence series in this collection has been processed, other parts are not yet fully processed. Nevertheless, this collection represents a very significant source of material regarding the rise of experimental embryology in the twentieth century. organizer.

Holtfreter's Life and Work

Born in 1901 in northern Germany, Hans Holtfreter would become one of the most influential experimental embryologists of the twentieth century. The son of a whiskey manufacturer, Holtfreter studied at the Universities of Rostock and Leipzig before arriving at the University of Freiburg where he studied under the renowned embryologist, Hans Spemann.

In 1924, while Holtfreter finished his doctorate on organogenesis in frog embryos, Hilde Proescholdt was performing a series of transplantation experiments that would lead Spemann to articulate his concept of the organizer. Proescholdt had taken cells from an amphibian embryo at the blastula stage just before gastrulation occurred and created different tissue layers and a body axis and transplanted them into another location on a second embryo. The second embryo then developed two separate body axes: one at the usual site and the second where the transplanted dorsal blastopore lip had been placed. Spemann's group determined that transplanted tissue had influenced the surrounding tissue to differentiate and form the second body axis. As a result, Spemann dubbed the dorsal blastopore lip region the organizer.

Holtfreter would eventually engage in organizer research, but he did not share Spemann's temperament or work habits. Upon graduation Spemann urged Holtfreter to continue his research at the Naples Zoological Station. Holtfreter went to Italy, but instead of pursuing embryological research, he wandered away from to the island of Ischia in the Bay of Naples, where he painted frescoes in the church in St. Angelo. Although Holtfreter was a very talented artist, he could not support himself with his art.

When he returned to Germany, having exhausted his personal funds, Holtfreter discovered how difficult it would be to find a position in science without Spemann's full endorsement. Teaching high school or becoming a fishery biologist on the remote island of Helgoland seemed like his only options. Fortunately, in 1928, Otto Mangold, who had been a student of Spemann's and Hilde Proescholdt's husband before her untimely death, had an opening at the Kaiser Wilhelm Institute for Biology in Berlin-Dahlem. He offered the job to Holtfreter, before consulting Spemann. Holtfreter accepted immediately and began one of the most scientifically productive periods of his life. In

Mangold's group, Holtfreter returned to the organizer. Unlike Spemann, who preferred to think of the organism as a whole, Holtfreter became interested in the specific developmental potential of different regions in isolation from the rest of the embryo. Using the glass needle technique perfected in the Spemann group, Holtfreter divided blastulas into many different parts and then followed the development of each region as it grew in isolation. These thousands of tissue explants had to survive long enough for any potential differentiation to be detected. Up to this point, embryos had been cultured in filtered water where they grew poorly and tended to become infected and die. In order to create better growing conditions, Holtfreter experimented with different saline solutions until he found a mixture that allowed embryonic tissue to survive and thrive. This solution became known as Holtfreter solution and was a crucial innovation that allowed Holtfreter and other embryologists to perform successful transplantation experiments.

As he explored the fate different regions, Holtfreter also began to question what it was about regions, such as the organizer, that allowed them to have such influence on surrounding tissues. Spemann thought the organizer's properties rested in features of its structure. Holtfreter thought that the organizer's effects may have nothing to do with living tissue and performed a series of transplantation experiments with killed organizer tissue. When this killed tissue induced the same effects as living tissue, Holtfreter concluded that the organizer's influence must be the result of an inducing substance—a chemical that diffused through surrounding tissue and determined its fate. This discovery started embryologists on a search for inducing substances and in effect began research on biochemical embryology.

Holtfreter's success at the Kaiser Wilhelm Institute was widely recognized. In 1934, he became an associate professor in the Zoology Department at the University of Munich. A year later, a Rockefeller Foundation Fellowship and a private travel grant allowed him to join Ross Harrison's laboratory at Yale University. Harrison and Spemann were collaborators and friends. Holtfreter knew Harrison and had agreed to study tissue culture in his lab when he accepted the fellowship. However, when he got to New Haven, he was much more interested in exploring New York city. Eventually, he left Harrison's lab and traveled across the United States and then on to Hawaii and Bali. Holtfreter lingered on Bali, which had a profound impact on him personally. When his funds ran low, he reluctantly completed his circumnavigation of the globe to return to Germany.

While Holtfreter had been immersed in his journey, Germany had undergoing its own transformation as the Nazi Party consolidated political power throughout the 1930s. Back in Germany, Holtfreter felt alienated, but he would soon find himself in more serious trouble. In 1938 accepted an invitation to speak at the Congress of Physics, Chemistry, and Biology at the International Exposition in Paris. As a German participant, the German government expected him to make hi presentation in German. Instead Holtfreter gave his paper in French. To make matters worse, he did not return immediately to Germany. With the honorarium from the Congress, he explored Algeria. The German government took notice and upon his return, he was denounced and imprisoned. Joseph Needham and many other friends arranged for his emigration. In 1939, he joined Needham's group at Cambridge University. Because he left for political reasons, Holtfreter was considered to be an enemy alien and was interred in a Canadian prison camp until 1942.

Holtfreter laws unable to do research as a prisoner and quickly became embittered. Using wooden shingles from the sides of the building in which he lived, he painted landscapes of his "Balinese dreamland." Realizing the great talent imprisoned nearby, officials at McGill University in Montreal began to arrange for the release of academic from the prison camps, John Berrill campaigned for Holtfreter's release and in 1944 Holtfreter joined the faculty at McGill.

Free to pursue embryology again, Holtfreter returned to the biology of gastrulation. The beautifully coordinated movements characteristic of gastrulation had been demonstrated by Walter Vogt ‘s technique of vital staining. Following Vogt, Spemann had seen gastrulation as the result of organism level organization and control. Holtfreter rejected this approach in favor of a more mechanistic perspective that emphasized physical forces and the actions of specific cells. By explanting different groups of cells, Holtfreter developed a new explanation of the mechanics of gastrulation based on the elongation of bottle cells to create an invagination and the surface tension produced by the coating of the blastula, which then drew in surrounding cells. The apparent coordination of cell movement was thus explained in physical-mechanical terms.

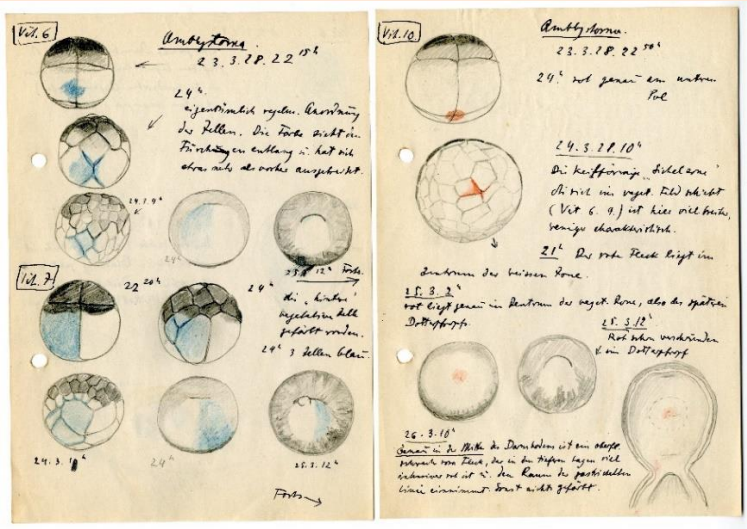
At McGill, Holtfreter continued to explore the physical and chemical influences on embryogenesis, especially the processes of neural development in early embryos. In 1941, Lester Barth demonstrated altering the concentration of salt in a solution could induce ectoderm to develop into neural tissue. Holtfreter extended Barth’s results by systematically adjusting the salt concentration and pH of solutions with presumptive neural ectoderm. Not only did Holtfreter induce this tissue to form neural tissue, they also formed rudimentary sensory organs. Because the tissue and solution used in these experiments did not include any organizer tissue, Holtfreter claimed that they demonstrated that neuralization was independent of the organizer and that, in fact, the salt solution facilitated autoneuralization by inhibiting the suppression of the capacity for neuralization inherent in the ectoderm.

While McGill freed him from an internment camp and allowed him to return to research, Holtfreter was never very happy there. One of Holtfreter’s close friends from Berlin, Curt Stern, had immigrated to the University of Rochester in New York. Eager to move to the United States, in 1946, Holtfreter took a position in Rochester, where he would stay until his death in 1992.

In Rochester, Holtfreter continued his work on the experimental embryology of amphibians. Most notably, he returned to an observation he had made in Germany about the affinity of different tissue types for each other. Ectoderm and endoderm did not have a strong affinity for each other, but mesoderm had a strong attraction to both ectoderm and endoderm. As cells became more differentiated this affinity grew stronger. In the 1950s Holtfreter and his student Philip Townes systematically studied this phenomenon of affinity and selective adhesion of cells. Townes and Holtfreter created mixtures of cells from different tissue layers and noted how they reassembled. They found that cells formed distinct tissue layers based on their affinities. This preferential movement and association led Holtfreter and Townes to conclude that cellular processes created the organization evident in the tissue layers of an embryo.

While Holtfreter’s research had a tremendous impact, in the United States, he was also partly responsible for the spread of the techniques of experimental embryology developed in the Spemann group. In the early 1950s, Holtfreter worked closely with his closest friend, Viktor Hamburger, to write the definitive overview of research on amphibian development for *The Analysis of Development*. Holtfreter and Hamburger had been friends since their student days in Spemann’s lab. Their joint chapter summarized the state of the art in experimental embryology as it reviewed the results that earned Spemann the Nobel prize, that launched biochemical embryology, and that made transplantation experiments the hallmark of experimental embryology in the twentieth century.

In 1968, Holtfreter retired from the University of Rochester. He spent his remaining days traveling with his spouse, Hiroka Ban Holtfreter, as well as painting and sketching until he lost his sight near the end of life.



Johannes Holtfreter's sketches of Amblystoma development. March 23 and 24, 1928.
Holtfreter Papers, Marine Biological Laboratory Archives, Woods Hole,

Holtfreter's Papers

In 2008, the Holtfreter collection was delivered to the Marine Biological Laboratory in 19 boxes. Historian Garland Allen worked with Holtfreter's widow, Hiroko, to donate selected professional correspondence, extensive laboratory notes, some manuscript drafts, as well as several 16 mm films and a projector for viewing those films. Holtfreter's art was distributed to collections in Rochester, NY and Richtenberg, Germany.

This collection is subdivided into correspondence, experiment notes, experiment illustrations, photographs, and films. The correspondence series has been curated and organized chronologically. Some notable correspondents have their own folders. Other parts of the collection will be processed at a later date. The collection has 16 linear feet of materials.

Correspondence

Most of the correspondence in this collection is from the post-war period. Notable correspondents include Holtfreter's close friend, Viktor Hamburger, Otto Mangold, Robert Briggs, Tuneo Yamada, Katsuma Dan, C. H. Waddington, Curt Stern, Richard Goldschmidt, and Jane Oppenheimer. There are some significant letters to and from family members from the 1930s, as well as letters regarding Holtfreter's immigration to England and the United States.

Notes

This collection contains an impressive set of laboratory notes. Holtfreter was forced to leave Cambridge, England very quickly when he was sent to a Canadian internment camp and entrusted his personal belongings to Hal Waddington. As Holtfreter notes in his letters, Waddington was less than diligent in keeping track of Holtfreter's things. Some of Holtfreter's personal belongings were lost, but not his laboratory records from Germany.

Beginning with five binders of notes from 1928 to 1933, Holtfreter's notes detail his experimental work on amphibian embryos, often hour by hour. These notes include his very important work on transplantation and explants. With some breaks, these notes continue from 1940 through the 1960s. Richly illustrated, these handwritten notes include descriptions in German and English, often with abbreviations. Yet, one can still pick out Holtfreter's experiments on gastrulation, surface tension, neurulation, cell inclusion, cell aggregation and cell movement.

Films

The Holtfreter collection includes 44 films and a film projector. I have not reviewed all of these films. Many seem to be from Holtfreter's trip to Japan in the 1960s when he was researching the movements and aggregation of slime molds. Others may be of his experiments on Amoebic movements in the 1970s.

Subject Files

When the collection was donated, it contained a few folders organized by subject. These included folders on Animals, Appointments, Habilitation, Immigration, Internment, and Travel. Holtfreter also collected a file of newspaper clippings in German, Japanese, and English. In his later years, he also engaged in some biographical reflections and was the subject of some biographical profiles. Drafts of this biographical material are also included in this collection.

Accessing the Collection

More information on the Holtfreter Collection is available online at: http://archives.mblwhoilibrary.org/repositories/3/resources/234.

The Marine Biological Laboratory Archives is located in the Lillie Building at the Marine Biological Laboratory at Woods Hole, MA. Because some material may be stored offsite, it is important to contact the archives before visiting.

Hours: 8 am to 5 pm, Monday through Friday
Contact: archives@mbl.edu
Phone: (508) 289-7341

Further Reading

Gerhart, John. "Johannes Holtfreter's Contribu

tions to Ongoing Studies of the Organizer." *Developmental Dynamics* 205 (1996): 245–256.

-----. "Johannes Holtfreter." *Biographical Memoirs of the National Academy of Science* 73 (1998): 3–22.

Gilbert, Scott, ed. *A Conceptual History of Modern Developmental Biology*. New York: Plenum Press, 1991.

Hamburger, Viktor. *The Heritage of Experimental Embryology: Hans Spemann and the Organizer*. New York: Oxford University Press, 1988.

Holtfreter, Johannes with H. Bautzmann, Hans Spemann, and Otto Mangold. "Versuche der Analyse der Induktionsmittel in der Embryonalentwicklung." *Naturwissenschaften* 20 (1932): 971–974.

----- "Veränderung der Reaktionsweise im altern den isolierten Gastrulaektoderm." *Roux' Archive für Entwicklungsmechanik* 138 (1938): 163–196.

------ "Differenzungspotenzen isolierter Teile der Anurengastrula." *Roux' Archive für Entwicklungsmechanik* 138 (1938): 657–738.

----- "A Study of the Mechanics of Gastrulation." Parts 1 and 2. *Journal of Experimental Zoology* 94 (1943): 261–318; 95 (1944): 171–212.

----- "Neural Differentiation of Ectoderm through Exposure to Saline Solution." *Journal of Experimental Zoology* 95 (1945): 307–340.

----- "Neuralization and Epidermization of Gastru la Ectoderm." *Journal of Experimental Zoology* 98 (1945): 169–209.

Holtfreter, Johannes and Viktor Hamburger. "Amphibians." In *Analysis of Development*, edited by B. H. Willier, P. A. Weiss, and V. Hamburger, 230–296. New York: W. B. Saunders, 1955.

Keller, Ray. "Holtfreter Revisited: Unsolved Problems in Amphibian Morphogenesis," *Developmental Dynamics* 205 (1996): 257–264.

Steinberg, Malcolm, and Scott Gilbert. "Townes and Holtfreter (1955): Directed Movements and Selective Adhesion of Embryonic Amphibian Cells." *Journal of Experimental Zoology* 301A (2004): 701–706.

Townes, P. and Johannes Holtfreter. "Directed Movements and Selective Adhesion of Embryonic Amphibian Cells." *Journal of Experimental Zoology* 123 (1955): 53–120.

The Richard Lewontin Papers at the American Philosophical Society

Charles Greifenstein
cgreifenstein@amphilsoc.org

IT has been fun to write pieces for the *Newsletter* as it lets me delve deeply into an important collection, recently acquired. Examples of these were the John M. Opitz papers (no. 20, 2015) and the Arno Motulsky papers (no. 16, 2007). The coronavirus crisis having forced the closing of the APS, I have not been to the Library since March, which puts me in an unfortunate position; I can't examine any collection. Nevertheless, I thought it worth making a stab at chronicling a recent acquisition: the Richard Lewontin papers. I remember enough about the collection, which I retrieved from Harvard in December 2018, to relate some sense of it, and there are particular circumstances about the papers that should be pointed out.

Lewontin was one of Dobzhansky's students at Columbia, where he received an MA in mathematical statistics and a PhD in zoology. After appointments at several institutions, Lewontin ended up at Harvard, where he spent the rest of his career. Now 91, he has emeritus status.

Training in mathematics provided Lewontin with the skills to make important contributions to population genetics and evolutionary biology. With Ken-Ichi Kojima he developed equations for change in haplotype frequencies and natural selection at two loci. His paper with Jack Hubby truly revolutionized population genetics by surveying loci in *Drosophila pseudoobsucra* using gel electrophoresis and demonstrating that many loci are polymorphic.

Richard Lewontin in his laboratory at Harvard University. No date. From personal collection of Michael R. Dietrich. Copied with permission from R. C. Lewontin.

For a population geneticist, Lewontin is widely known, and became more so as his writing and speaking developed into social commentary. His profile rose with such work as his on race, arguing in a paper, for instance, that race classification is of little meaning given its small part in human genetic variability. He has also argued that organisms do not exist passively in their environment but also ac-

tively shape the environment for future generations. His most visible public activity is as being a critic of social biology, which explains behavior and social arrangements as evolutionarily advantageous. Lewontin questions the heritability of human traits, such as intelligence, faulting IQ testing as an inadequate measure of it. Germany.

The papers at the APS cover Lewontin's long and significant career. They in fact arrived at the APS in more than one accession. The first (4 linear feet) was in 1979 when he deposited copies of a good deal of important correspondence. Familiar names abound: Crow, Delbrück, Dobzhansky, Haldane, Mayr, Neel, Wright. Two smaller of accessions assorted material and cassette recordings arrived in 2003. I drove a van up to Cambridge to pick up the rest in 2018.

The papers were kept in a room Vanserg Hall, pretty much by themselves. There were 11 file cabinets and assorted banker's boxes. With the help of Steve Orzack and Diane Paul, I packed up 108 linear feet of material.

One cabinet held manuscripts of Lewontin's work. I have not examined these files specifically, but they appear pretty comprehensive. There were many draws with copies of the printed work. About 5 cabinets held reprints of others' work, a huge amount. I would have preferred to go through these discard photocopies and commonly-available reprints, but time did not permit. At any rate some reprints now are growing in value, so examining them could yield surprises. They were removed from their hanging folders and kept in alphabetical order. The banker's boxes held some of Lewontin's early research notebooks.

Some four cabinets held correspondence, the meat of the papers. There is much interesting material in the correspondence, but folders have been removed by the Harvard University Archives. University policy states that "access to University administrative records [is restricted] for a period of 50 years from the date of their creation. University records pertaining to individuals, including student and employee records, are closed for a minimum of 80 years." While "Personal archives of faculty, administrators, students, and alumni/ae may be subject to restrictions established by the donor. University records in personal archives are subject to the same 50- and 80-year restrictions on access required by University policy."[1]

Folders were removed according to 28 criteria.[2] Each folder removed was marked with a form indicating the folder title and the reason it was removed. As far as I know, the contents of each folder were not fully vetted before its removal. A folder, for instance, could have had a name on it of an individual who worked in Lewontin's lab and later was a correspondent and collaborator. That folder would be removed as it could contain employee or fellowship records. If a folder was marked "Oa-Op" and there was something in the folder meeting the criteria, the whole folder was removed without examination.

The APS usually allows access to papers when they arrive, as long as they have been examined and are partially organized. Because the Lewontin papers that were kept in the cabinets were boxed in original order and were arranged alphabetically, access is possible through the Curator of Manuscripts.

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[1] See https://library.harvard.edu/how-to/access-materials-harvard-university-archives.

[2] Noted on a document sent to Charles Greifenstein by Harvard University Archives, August 2018.